Managing Outpatient Parenteral Antimicrobial Therapy

Infectious Diseases Society of America Revises Clinical Practice Guideline

By Jeannie Counce and Nabin K. Shrestha, MD, MPH, FACP, FIDSA

PHARMACISTS AND PHARMACY TECHNICIANS

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www.nhia.org/CE_Infusion

March/April 2019
Learning Objectives:
1. Differentiate between the three major models for delivering outpatient parenteral antibiotic therapy (OPAT)
2. Understand the role of the infectious disease expert in prescribing and monitoring OPAT therapy as described in the guideline.
3. List five significant changes/updates in the 2018 OPAT practice guideline compared to the 2004 version.
4. Differentiate between the type of patients who are recommended for home OPAT therapy under the guideline versus those for which there are no recommendations.

Introduction and Background
In November 2018, the Infectious Diseases Society of America (IDSA) released a new clinical practice guideline on outpatient parenteral antimicrobial therapy (OPAT), which was published in Clinical Infectious Diseases. The new guideline was intended to provide insight for health care professionals who prescribe and oversee the provision of OPAT.

This revision, which updates the guideline published in 2004¹, focuses on a review of the literature to answer specific OPAT practice questions. To do this, IDSA convened a panel of experts who followed a process of systematic weighting of the evidence found, using that to rate the strength of each recommendation and the quality of evidence used to reach it (see Exhibit 1).

The guideline considers various patient features, infusion catheter issues, monitoring questions, and antimicrobial stewardship concerns. It is not intended to replace clinical judgment in the management of individual patients. A detailed description of the methods, background, and evidence summaries that support each recommendation can be found in the full text of the guideline, which is available online at https://doi.org/10.1093/cid/ciy745.

Exhibit 1
Rating System for Recommendations and Evidence Quality in IDSA Clinical Practice Guideline

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Evidence Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>No recommendation</td>
<td>No Evidence</td>
</tr>
<tr>
<td>Weak recommendation</td>
<td>Very Low</td>
</tr>
<tr>
<td>Strong recommendation</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>High</td>
</tr>
</tbody>
</table>

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AUTHOR DISCLOSURE STATEMENT
The authors declare no conflict of interest or financial interest in any product or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

www.nhia.org/CE_Infusion
Outpatient parenteral antimicrobial therapy (OPAT) is defined as the administration of parenteral antimicrobial therapy in at least two doses on different days without an intervening hospitalization. The positive outcomes associated with OPAT in various populations and settings are well documented.\(^2\) OPAT also offers potential benefits to the health care system, including reduced or avoided hospital stays,\(^8,9\) prevention of hospital-associated conditions,\(^10\) and significant cost savings.\(^2,10-17\) Patients can benefit from OPAT as well, because it offers the ability to return to work or school sooner, care for children or dependents, and resume activities of daily living with minimal interruption.\(^18,19\)

OPAT is typically delivered in one of three basic models (see Exhibit 2) with the ongoing majority of patients receiving therapy in the home site of care.\(^20\) There are several factors to consider when selecting the appropriate site of care for an individual patient. These include: payer type, available resources (access to home nursing specializing in infusion; hours of operation for infusion suites may not include weekends or evenings), as well as patient preference, competencies, and level of support. [Editor’s Note: Medicare coverage of anti-fective therapies is woefully inadequate. NHIA is working to address coverage issues for these and all infusion therapies delivered in the home and outpatient infusion center. Please visit www.nhia.org/Part_B_Reimbursement/index.html to learn more.]

Advances in infusion device technology have made it possible to administer almost any antimicrobial medication in the outpatient setting, therefore, choosing the appropriate therapy now depends more on the delivery model and medication stability than on the pharmacokinetic properties of the drug. The updated guideline, which is arranged in a Question-Recommendation format, includes tables on many antimicrobial agents and details about administration methods, infusion time, oral bioavailability, laboratory monitoring recommendations, and adverse drug reactions. Non–laboratory-based toxicities that inform monitoring strategies are also included.

**Home Administration of OPAT**
A key take-away from the 2018 guideline is that OPAT administered at home by patients or caregivers is safe and effective. OPAT has long been the standard of care to treat an infection that requires IV antimicrobials because it is less expensive than hospital-based treatment and is preferred by most patients. Since the previous guideline was published in 2004, three large studies have found this strategy to be safe. There is no difference in readmission rates or the number of adverse events related to OPAT administered by patients or their non-medical caregivers compared to health care worker-administered IV antimicrobial therapy.\(^21,23\)

The guideline supports patient/caregiver administration of OPAT in the home with or without a clinician present as long as there is a system in place for effective monitoring for vascular access complications and antimicrobial adverse events (Questions 1 and 2). The guideline also supports elderly patients receiving OPAT in the home assuming that potential challenges to OPAT in this patient population, such as cognition, mobility, and dexterity, have been considered and that the patient or caregiver is able to communicate with the treatment team if necessary (Question 4).

Due to a lack of evidence, the panel declined to make a recommendation on whether or not persons who inject drugs should be treated with OPAT at home, given the risk of misuse of IV access (Question 3). Likewise, the panel declined to make a recommendation regarding OPAT treatment for infants younger than one month of age (Question 5). Clinicians are advised to make those decisions on a case-by-case basis.

The new guideline supports administering first doses of IV antimicrobials in the home provided the patient has no history of allergy to antimicrobials in the same class (Question 6). The administration should be performed under the supervision of a health care worker who is trained to manage an anaphylactic reaction. In 2016, NHIA released a guide to help clinicians manage acute infusion reactions in the home. This guideline can be accessed at http://digitaleditions.sheridan.com/publication/?i=293773&ver=html5&p=40.

The updated guideline includes more information on the selection of vascular access devices (VAD) for OPAT. The recommendations now allow for midline catheters, rather than central catheters, in adult patients needing short courses (less than 14 days) of antimicrobial therapy (Question 7). Another change is that it is no longer necessary to remove a vascular access device if a patient develops catheter-associated venous thromboembolism (CA-VTE) during OPAT, as long as the catheter remains well positioned and arm pain and swelling decrease with anticoagulation (Question 11).

**Role of the Infectious Disease Expert**
The new guideline stresses the valuable role of the infectious disease (ID) expert. It recommends that each case be reviewed by an ID expert—physician, nurse, or pharmacist—before therapy
is initiated (Question 17). This step can limit the unnecessary use of parenteral therapy (when oral will suffice), improve care coordination, and enhance antimicrobial stewardship. One study found an ID specialist-led stewardship program reduced pediatric OPAT orders by 24%, without increasing readmissions.²⁴

The guideline emphasizes that correct treatment begins with an accurate diagnosis and calls for proper identification of the infection to be treated and selection of an appropriate antimicrobial agent. ID experts would be expected to have an understanding of the primary site of infection, the extent of infection around the primary site, and distant sites seeded secondarily. Other factors involved in selecting the appropriate antimicrobial agent include: patient co-morbidities, concomitant therapies (drug and non-drug), patient age, organ function, dosing schedule, drug stability, and vascular access device.

Once patients begin receiving OPAT, the guideline recommends that they should be monitored regularly (Question 14). Newer research also supports the assertion that patients should have regular blood tests while receiving OPAT to monitor for toxicity and ensure that drug levels are within the therapeutic range.²⁵⁻²⁷ Although there is no definitive evidence regarding how often that should occur, most patients are tested weekly. Monitoring is especially critical for patients who are being treated with vancomycin therapy (Question 15). Vancomycin levels should be monitored closely throughout the course of treatment as one study found 42% of patients developed nephrotoxicity (kidney damage) after the 14th day on

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### Exhibit 2

**Models of Care for OPAT**

<table>
<thead>
<tr>
<th>Medications Administered By</th>
<th>Home</th>
<th>Infusion Center</th>
<th>Skilled Nursing Facility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Patient</td>
<td>• Health care workers</td>
<td>• On-site nurses</td>
</tr>
<tr>
<td></td>
<td>• Caregiver</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Home health nurse</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Description                  |                                           |                                                                          |                                                                                        |
|                             | • Patient education in the home on first visit or in a physician’s office | • No patient/caregiver training                                             | • No patient/caregiver training                                                       |
|                             | • Weekly nursing visits in home—or patient visits to physician’s office—for supplies, line care, and labs | • Infusions delivered in physician’s office or freestanding infusion center | • Infusions delivered in an inpatient setting                                           |
|                             | • Clinical troubleshooting 24/7           |                                                                           |                                                                                        |

| Advantages                  |                                           |                                                                          |                                                                                        |
|                             | • Patient convenience                     | • Good for patients who are physically incapable or unwilling to self-infuse | • Good for patients with additional medical needs (wound care, physical therapy, etc.) who lack caregiver support and/or are not ambulatory. |
|                             | • Regular clinical assessments            | • Offers increased clinical observation                                   | • Coverage exists for patients who lack home infusion insurance coverage (i.e. Medicare) |
|                             | • Allows patient to return to work/school, and resume normal activities | • Good for patients who lack home infusion insurance coverage (i.e. Medicare) |                                                                                        |

| Disadvantages               |                                           |                                                                          |                                                                                        |
|                             | • Requires patient/caregiver competence and compliance | • Requires more clinical resources (nursing for every infusion, weekend/holiday staffing) | • Increases patient risk of encountering resistant organisms                         |
|                             | • Patient may incur costs, depending on insurance coverage. Commercial insurance and Medicaid, usually cover therapy with a co-payment. Medicare coverage is inadequate, forcing patients to pay large out-of-pocket expenses, or receive care in a SNF, or make daily trips to an outpatient infusion center | • Requires patient to travel to and from site of care for each dose               | • Patient inconvenience due to inpatient stay                                        |
|                             |                                           | • Patient inconvenience                                                  | • May exhaust patient’s SNF benefits                                                 |
|                             |                                           | • Interferes with work/school, daily activities                          | • Significantly more expensive to health care system                                 |

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If nephrotoxicity develops, options include lowering the dose or stopping the vancomycin and switching to another medication such as daptomycin. The multi-disciplinary home infusion therapy team, which includes a pharmacist, is adept at monitoring patients on vancomycin for adverse events and maximum efficacy and consulting with ID physicians if/when treatment regimens should be adjusted. The full text of the guideline is available on the IDSA website at https://academic.oup.com/cid/article/68/1/e1/5175018. Below are three case studies that highlight the most significant changes in the updated guideline as they might pertain to patients being treated by home infusion therapy providers.

Case 1

A 51-year-old man with a prosthetic knee joint infection due to methicillin-susceptible Staphylococcus aureus underwent removal of the prosthesis and placement of an antibiotic-impregnated spacer as a stage 1 of a two-stage revision. He was discharged home (a 5-hour drive away) on IV oxacillin and home physical therapy three days after surgery. After eight days, the patient, who had no history of allergy, developed a generalized maculopapular rash. Complete blood count and serum creatinine checked the previous day had been normal. The patient sent a picture of the rash to his infectious disease (ID) physician who decided to replace oxacillin with vancomycin.

What should you do next?

1. Bring the patient back in to clinic to administer the first dose of vancomycin.
2. Send the patient to a local emergency department so he can be evaluated and antibiotic changes made as necessary.
3. Have the patient find a local ID physician who would be willing to see the patient and make antibiotic adjustments.
4. Administer vancomycin in the patient’s home.

2004 Guideline

“The initial dose of an intravenous agent should be administered in a supervised setting, such as a physician’s office, ambulatory care department, or the hospital, before a patient’s discharge to home care.”

2018 Guideline

Question 6 – Is it safe and appropriate to administer the first OPAT dose of a new antimicrobial at home?

Recommendation – In patients with no prior history of allergy to antimicrobials in the same class, the first dose of a new parenteral antimicrobial may be administered at home under the supervision of health care personnel who are qualified and equipped to respond to anaphylactic reactions (weak recommendation, very low-quality evidence).
Case 2

A 48-year-old woman was hospitalized with a right upper quadrant intra-abdominal abscess associated with Enterococcus faecalis bacteremia. The abscess was drained via a catheter placed with CT-guidance; the patient improved and the bacteremia cleared. She was discharged from the hospital after 5 days with a plan to complete a 14-day course of treatment with a peripherally inserted central catheter (PICC) for vascular access. Three days after discharge, the patient presented to the emergency department with pain and swelling in the arm harboring the PICC. Venous duplex found deep vein thrombosis in the basilic, axillary, and subclavian veins of the arm.

What should you do next?

1. Remove the vascular access device from this patient.
2. Remove the vascular access device and admit patient for further workup and evaluation.
3. Access the vascular access device for position and redness/swelling and begin anticoagulation.

2004 Guideline

“The development of ipsilateral edema of the neck or arm in association with a PICC or other central catheter should prompt evaluation for a deep vein thrombosis, which usually requires removal of the device.”

2018 Guideline

**Question 11** – Should the vascular access device be removed if a patient develops symptomatic catheter-associated venous thromboembolism (CA-VTE) while on OPAT?

**Recommendation** - It is not necessary to remove a vascular access device if CA-VTE develops during OPAT, as long as the catheter remains well-positioned and arm pain and swelling decrease with anticoagulation (weak recommendation, very low-quality evidence).

**Question 12** – Should patients with prior CA-VTE be treated with prophylactic anticoagulation while on OPAT?

**Recommendation** - No recommendation can be made regarding the need to treat patients with a history of prior CA-VTE with prophylactic oral anticoagulation while on OPAT (no recommendation, no evidence).

Case 3

A 54-year-old man with a prosthetic aortic valve was admitted to the hospital with methicillin-resistant Staphylococcus aureus bacteremia. He was found to have prosthetic valve endocarditis with an aortic root abscess. The patient was taken for surgery and the aortic valve and root were replaced with a homograft. The patient had an uneventful recovery. Seven days after surgery, he was discharged home (a 2-hour drive away) on IV oxacillin with a plan to complete a 6-week course of treatment. How often should he be seen by his ID physician or the ID service?

What should you do next?

1. Due to the diagnosis of endocarditis, he is not a suitable candidate for home infusion, and should return to hospital to be placed in a skilled nursing facility for physician oversight.
2. Make weekly appointments at the physician’s office for labs, vascular access device care, and physical assessment by the physician.
3. Assess the patient’s infection, co-morbid disease states, and socio-economic condition to determine best plan for physician follow up appointments.

2004 Guideline

“In most circumstances, patients see the managing physician once or twice each week. Some patients need to be seen daily by a physician, especially at the beginning of OPAT. Patients with endocarditis, meningitis, or other life-threatening infections may also require more frequent visits.”

2018 Guideline

**Question 16** – How frequently should patients on OPAT have scheduled physician office visits for monitoring of treatment?

**Recommendation** - No generalized recommendation on frequency of outpatient follow-up can be made for patients treated with OPAT (no recommendation, no evidence). The frequency of office visits should be dictated by the treating physicians, giving consideration to patient characteristics, the nature of the infection, the patient’s tolerance of and response to therapy, and individual patient social factors.

**Question 17** – Should all patients have ID expert review prior to initiation of OPAT?

**Recommendation** - All patients should have ID expert—physician, pharmacist, or nurse—review prior to initiation of OPAT (strong recommendation, very low-quality evidence).
Conclusion

Outpatient administration of IV antibiotics has been proven to be safe and effective with multiple benefits to patients and the health care system. With this guideline revision, IDSA broadens this statement to include elderly patients. Aside from the challenges presented by Medicare coverage of OPAT, the home is considered a cost-effective site of care that allows patients to be engaged in regular daily activities and reduce their risk of coming into contact with drug-resistant organisms.

The new guideline also stresses the importance of the ID expert—physician, pharmacist, or nurse—in prescribing and monitoring therapy. Having a member of the clinical team with this level of expertise improves outcomes and contributes to overall efforts to improve antimicrobial stewardship. The clinical teams—pharmacists, nurses, and others—that deliver home infusion therapy are well-versed in caring for these patients, monitoring patient progress, and collaborating with prescribers to ensure positive outcomes.

References